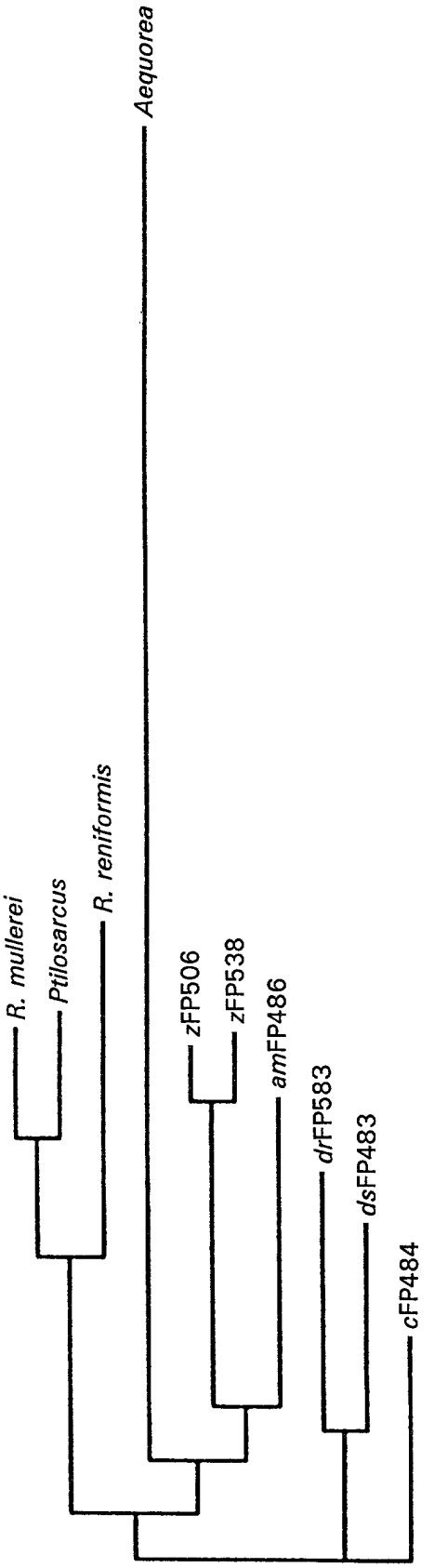
Aequorea
R. reniformis
Ptilosarcus
R. mullerei
zFP506
zFP538
amFP486
drFP583
dsFP483
cFP484

FIG. 1

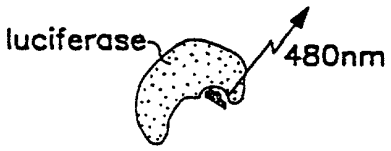

FIG. 2A

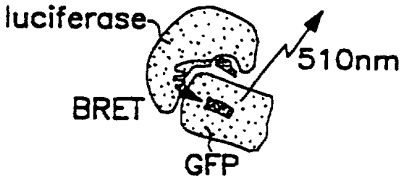

FIG. 2C

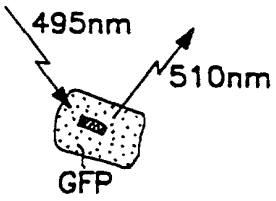

FIG. 2B

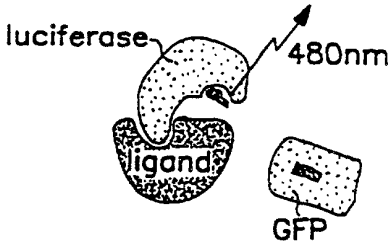

FIG. 2D

BRET Sensor Architectures

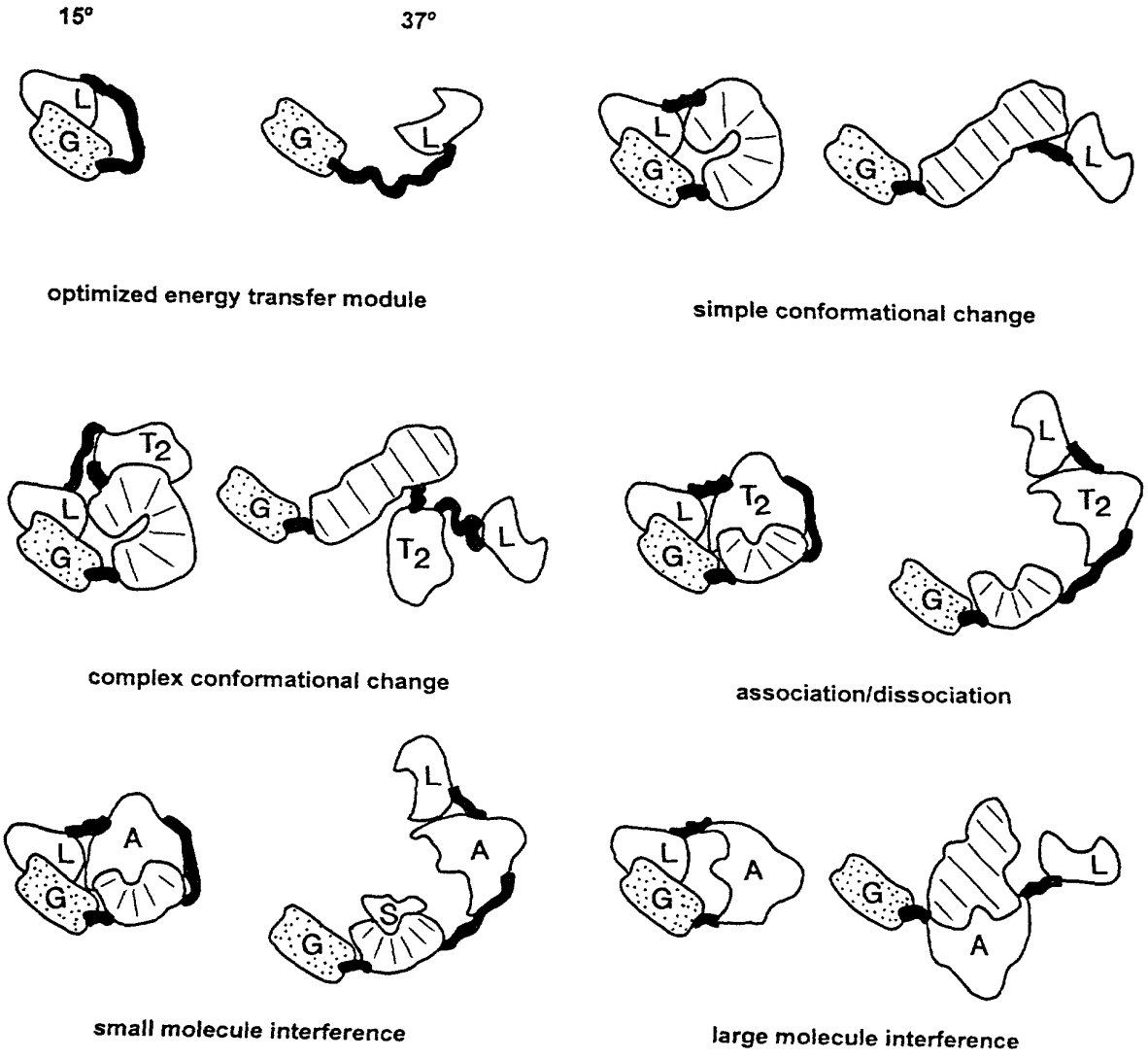

FIG. 3

Utilization of advantageous GFP surfaces with substituted fluorophores

```
                  60          *          80
RM-GFP    :   GAPLPFAFDIVSPAFQYGNRTFTKYPNDIS--    :   83
Pt-GFP    :   GGPLPFAFDIVSIAFQYGNRTFTKYPDDIA--    :   83
RR-GFP    :   GAPLPFAFDIVSVAFSYGNRAYTGYPEEIS--    :   80
cFP484    :   GAPLPFSYDILSNAFQYGNRALTKYPDDIA--    :   83
drFP583   :   GGPLPFAWDILSPQFQYGSKVYVKHPADIP--    :   80
asFP595   :   GGPLPFAFHILSTSCMYGSKTFIKYVSGIP--    :   77
dsFP483   :   GGPLPFGWHILCPQFQYGNKAFVHHPDNIH--    :   80
amFP486   :   GGPLAFSFDILSTVFKYGNRCFTAYPTSMP--    :   82
zFP506    :   GGPLPFAEDILSAAFNYGNRVFTEYPQDIV--    :   80
zFP538    :   GGPLPFSEDILSAGFKYGDRIFTEYPQDIV--    :   80
              ====================
```

FIG. 4

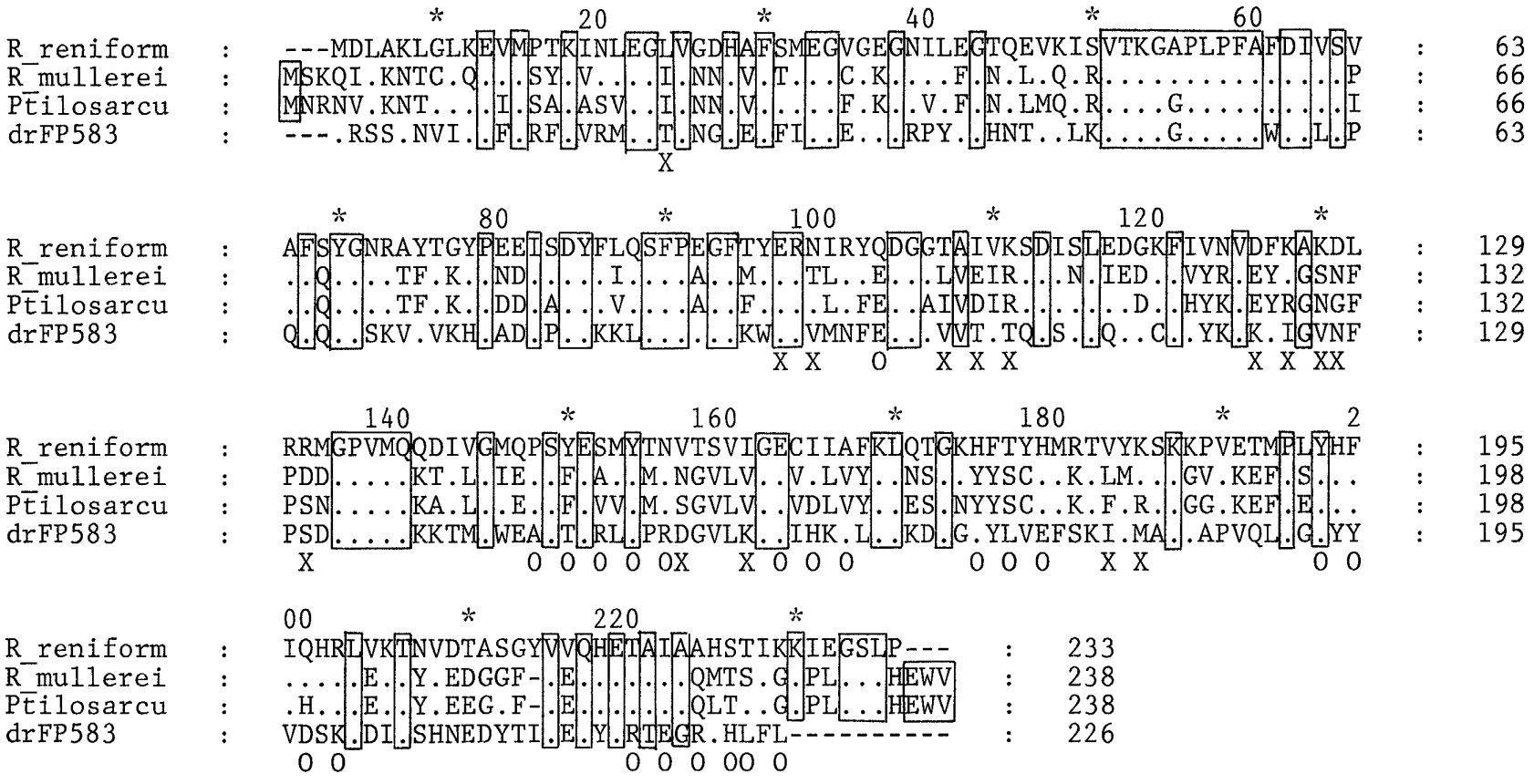

FIG. 5

```
                  *       20        *       40        *       60        *       80
Aequorea    : ---MSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLKFICTT---GKLPVPWPTLVTTFSYGVQCFSRYPDHMK :  79
R_mullerei  : MSKQILKNTCLQEVMSYKVNLEGIVNNHVFTMEGCGKGNILFGNQLVQIRVTK--GAPLPFAFDIVSPAFQYGNRTFTKYPNDI- :  82
Ptilosarcu  : MNRNVLKNTGLKEIMSAKASVEGIVNNHVFSMEGFGKGNVLFGNQLMQIRVTK--GGPLPFAFDIVSIAFQYGNRTFTKYPDDI- :  82
R_reniform  : ---MDLAKLGLKEVMPTKINLEGLVGDHAFSMEGVGEGNILEGTQEVKISVTK--GAPLPFAFDIVSVAFSYGNRAYTGYPEEI- :  79
drFP583     : ---MRSSKNVIKEFMRFKVRMEGTVNGHEFEIEGEGEGRPYEGHNTVKLKVTK--GGPLPFAWDILSPQFQYGSKVYVKHPADI- :  79
drFP593     : ---MSCSKNVIKEFMRFKVRMEGTVNGHEFEIKGEGEGRPYEGHCSVKLMVTK--GGPLPFAFDILSPQFQYGSKVYVKHPADI- :  79
dsFP483     : ---MSCSKSVIKEEMLIDLHLEGTFNGHYFFIKGKGKGQPNEGTNTVTLEVTK--GGPLPFGWHILCPQFQYGNKAFVHHPDNI- :  79
cFP484      : --KALTTMGVIKPDMKIKLKMEGNVNGHAFVIEGEGEGKPYDGTHTLNLEVKMAEGAPLPFSYDILSNAFQYGNRALTKYPDDI- :  82
asFP595     : ------MASFLKKTMPFKTTIEGTVNGHYFKCTGKGEGNPFEGTQEMKIEVIE--GGPLPFAFHILSTSCMYGSKTFIKYVSGI- :  76
amFP486     : ---MALSNKFIGDDMKMTYHMDGCVNGHYFTVKGEGNGKPYEGTQTSTFKVTMANGGPLAFSFDILSTVFKYGNRCFTAYPTSM- :  81
zFP538      : ---MAHSKHGLKEEMTMKYHMEGCVNGHKFVITGEGIGYPFKGKQ--TINLCVIEGGPLPFSEDILSAGFKYGDRIFTEYPQDI- :  79
zFP506      : ---MAQSKHGLTKEMTMKYRMEGCVDGHKFVITGEGIGYPFKGKQ--AINLCVVEGGPLPFAEDILSAAFNYGNRVFTEYPQDI- :  79

                 *       100        *       120        *       140        *       160        *
Aequorea    : RHDFFKSAMPEGYVQERTIFFKDDGNYKTRAEVKFEG--DTLVNRIELKGIDFKEDGNILGHKLEYNYNSHNVYIMADKQKNGIK : 162
R_mullerei  : -SDYFIQSFPAGFMYERTLRYEDGGLVEIRSDINLIE--DKFVYRVEYKGSNFPDDGPVMQKTI-LGIEPSFEAMYM--NNGVLV : 161
Ptilosarcu  : -ADYFVQSFPAGFFYERNLRFEDGAIVDIRSDISLED--DKFHYKVEYRGNGFPSNGPVMQKAI-LGMEPSFEVVYM--NSGVLV : 161
R_reniform  : -SDYFLQSFPEGFTYERNIRYQDGGTAIVKSDISLED--GKFIVNVDFKAKDLRRMGPVMQQDI-VGMQPSYESMYT--NVTSVI : 158
drFP583     : -PDYKKLSFPEGFKWERVMNFEDGGVVTVTQDSSLQD--GCFIYKVKFIGVNFPSDGPVMQKKT-MGWEASTERLYP--RDGVLK : 158
drFP593     : -PDYKKLSFPEGFKWERVMNFEDGGVVTVSQDSSLKD--GCFIYEVKFIGVNFPSDGPVMQRRT-RGWEASSERLYP--RDGVLK : 158
dsFP483     : -HDYLKLSFPEGYTWERSMHFEDGGLCCITNDISLTG--NCFYYDIKFTGLNFPTNGPVVQKKT-TGWEPSTERLYP--RDGVLI : 158
cFP484      : -ADYFKQSFPEGYSWERTMTFEDKGIVKVKSDISMEE--DSFIYEIRFDGMNFPPNGPVMQKKT-LKWEPSTEIMYV--RDGVLV : 161
asFP595     : -PDYFKQSFPEGFTWERTTTYEDGGFLTAHQDTSLDG--DCLVYKVKILGNNFPADGPVMQNKA-GRWEPATEIVYE--VDGVLR : 155
amFP486     : -PDYFKQAFPDGMSYERTFTYEDGGVATASWEISLKG--NCFEHKSTFHGVNFPADGPVMAKKT-TGWDPSFEKMTV--CDGILK : 160
zFP538      : -VDYFKNSCPAGYTWGRSFLEEDGAVCICNVDITVSVKENCIYHKSIFNGMNFPADGPVMKKMT-TNWEASCEKIMPVPKQGILK : 162
zFP506      : -VDYFKNSCPAGYTWDRSFLFEDGAVCICNADITVSVEENCMYHESKFYGVNFPADGPVMKKMT-DNWEPSCEKIIPVPKQGILK : 162

               180        *       200        *       220        *       240        *
Aequorea    : VNFKIRHNIEDGSVQLADHYQQNTPIG-DGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGITHGMDELYK---- : 238
R_mullerei  : GEVILVYKLNSGKYYSCHMKTLMKSKG--VVKEFPSYHFIQHRLEKTYVEDGGF--VEQHETAIAQMTSIGKPLGSLHEWV : 238
Ptilosarcu  : GEVDLVYKLESGNYYSCHMKTFYRSKG--GVKEFPEYHFIHHRLEKTYVEEGSF--VEQHETAIAQLTTIGKPLGSLHEWV : 238
R_reniform  : GECIIAFKLQTGKYFTYHMRTVYKSKK--PVETMPLYHFIQHRLVKTNVDTASG-YVVQHETAIAAHSTIKKIEGSLP--- : 233
drFP583     : GEIHKALKLKDGGHYLVEFKSIYMAKK--APVQLPGYYYVDSKLDITSHNEDYT-IVEQYERTEGRHHLFL---------- : 226
drFP593     : GDIHMALRLEGGGHYLVEFKSIYMVKK--PSVQLPGYYYVDSKLDMTSHNEDTY-VVEQYEKTQGRHHPFIKPLQ------ : 230
dsFP483     : GDIHHALTVEGGGHYACDIKTVYRAKK--AALKMPGYHYVDTKLVIWNNDKEFM-KVEEHEIAVARHHPFYEPKKDK---- : 232
cFP484      : GDISHSLLLEGGGHYRCDFKSIYKAK---KVVKLPDYHFVDHRIEILNHDKDYN-KVTLYENAVARYSLLPSQA------- : 231
asFP595     : GQSLMALKCPGGRHLTCHLHTTYRSKKPASALKMPGFHFEDHRIEIMEEVEKGK-CYKQYEAAVGRYCDAAPSKLGHN--- : 232
amFP486     : GDVTAFLMLQGGGNYRCQFHTSYKTK---KPVTMPPNHVVEHRIARTDLDKGGN-SVQLTEHAVAHITSVVPF-------- : 229
zFP538      : GDVSMYLLLKDGGRYRCQFDTVYKAK--SVPSKMPEWHFIQHKLLREDRSDAKNQKWQLTEHAIAFPSALA---------- : 231
zFP506      : GDVSMYLLLKDGGRLRCQFDTVYKAK--SVPRKMPDWHFIQHKLTREDRSDAKNQKWHLTEHAIASGSALP---------- : 231
```

D,E,H,K,R	N,Q,S,T	L,I,V,M,F,Y,W	A,G	C,P
polar charged	polar uncharged	non-polar hydrophobic	small	not grouped

dimerization surfaces	
☐	hydrophilic
☐	hydrophobic

FIG. 6